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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/463,352 01/21/00 GOUDSMIT

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EXAMINER

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ART UNIT

PAPER NUMBER

1655

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/463,352	GOUDSMIT ET AL.
	Examiner Bradley L. Sisson	Art Unit 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 15 June 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-9, 11 and 12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-9, 11 and 12 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____ .
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
- 4) Interview Summary (PTO-413) Paper No(s) _____ .
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-9, 11, and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Montagnier et al., in view of Research Genetics.

Montagnier et al., column 19, third paragraph, bridging to column 20, disclose primers for detecting HIV-1 and methods of doing same. At column 19, last paragraph, bridging to column 20, first two lines, Montagnier et al., teach explicitly of directing primers to conserved regions and specifically teaches that one such region of conserved sequences is found in the long

terminal repeat, or LTR. It is noted that the LTR is the very region from which applicant has selected the instantly claimed primers/probes; see the response of 26 December 2000, page 7, lines 13-15, wherein is stated:

The primers of the present invention are not from the GAG region, but instead are from the long terminal repeat (LTR) of HIV-1."

It is abundantly clear that Montagnier et al., are directing the public to this very region for the selection of primers and probes. Furthermore, they provide motivation in selecting sequences that allow for the detection of multiple isolates when they teach that the LTR is "highly conserved."

Montagnier et al., column 20, second paragraph, teach that RT-PCR can be practiced and that such allows for the detection of viral sequences in individuals before they seroconvert.

Research Genetics, through their advertisement, disclose for sale software that allows the ordinary artisan to set parameters whereby the software will automatically screen all possible sequence comparisons and provide a listing of those primers that meet the established criteria. As seen in the publication, such parameters to be employed in the selection of primer and probe sequences include desired specificity, length, GC content, secondary structure characteristics, etc.

It would have been obvious to one of ordinary skill in the art at the time the instantly claimed invention was made to have used the software of Research Genetics with the teachings of Montagnier et al., so to select primers and probes form the LTR region of HIV-1 where such sequences are identified through the use of the commercially available sequence screening software. With Montagnier et al., teaching explicitly to identify and make primers that in turn

comprise highly conserved HIV-1 LTR sequences, as well as the use of such primers in PCR reactions, and with the straightforward, Windows-based software allowing for the ready identification of just such conserved sequences between isolates, the skilled artisan would have reasonably expected to have identified primers of an appropriate length and which are comprised of the now claimed conserved nucleotide sequence. Said artisan would have been motivated to have used primers that anneal to highly conserved HIV-1 LTR regions as Montagnier et al., explicitly teaches performing PCR on HIV-1 as well as the production of primers directed to highly conserved HIV-1 LTR regions.

Applicant's statements to their ability to detect all known isolates of HIV-1 through the use of their primers/probes, in light of the explicit teachings of Montagnier et al., do not rise to the level of a an unexpected and non-obvious quality. Additionally, the claims, as presently written, do not support the assertion of any unexpected result. It is noted with particularity that the primers are to be (a) derived from SEQ ID NO:1-5 and 12, and that they can be from 10-50 nucleotides in length. None of the sequences represented by SEQ ID NO:1-5 or 12 are 50 nucleotides in length. As seen below in the following chart, the sequences set forth in the claims, e.g., claim 1, are all far short of the claimed upper length allowed for the primers.

SEQ ID NO.	Length	No. of Additional Nucleotides that can be Added
1	18	32
2	20	30
3	15	35
4	20	30
5	20	30
12	30	20

It is noted with particularity that with the primers being anywhere from 10 to 50 nucleotides in length, any with there being a minimum of 10 nucleotides being used from each of SEQ ID NO:1-5 and 12, the claims encompass a nearly limitless number of probes . Support for this position is based in part on the claims encompassing primers of 50 nucleotides in length yet only 10 of the nucleotides being from any one of the sequences represented by a SEQ ID NO., e.g., SEQ ID NO:1. Accordingly, and using for example a probe of 50 nucleotides in length, and with there being 9 possible 10mers derived from SEQ ID NO:1, there are 9×4^{40} or 1.08×10^{28} possible probes. The number of probes is compounded even further when one contemplates the number of possible probes when the number of nucleotides added can range from 1 to 39, and then to recompute for 11mers, 12mers, etc., being derived from just SEQ ID NO:1, and then start anew for SEQ ID NOS: 2, 3, 4, 5, and 12. Clearly, the evidence of record is insufficient to support that such an immense genus of sequences, as a whole, exhibit an unusual or unexpected property.

To further cast doubt on the inability of the majority of the members of the genus to exhibit an unexpected property, attention is directed to the publication of Sommer and Tautz which show that effective priming was achieved with as little as three nucleotides matching at the 3' end of the primer. In light that there is no requirement that the additional 1 to 40 nucleotides added to the essential 10mer not be from HIV-1, much less a conserved region of an LTR of HIV-1, the likelihood of irrelevant sequences imparting the asserted unexpected property is most unlikely.

Accordingly, the rejection under 35 USC 103(a) has not been found to be lessened by a secondary consideration.

Response to argument

At page 1, last paragraph, bridging to page 2 of the response of 15 June 2001, hereinafter the response, it is asserted that the above rejection does not render the claims *prima facie* obvious as the claims are drawn to particular probes rather than to probes generally. This argument has been fully considered and has not been found persuasive for as shown above, the claims are not drawn to 8 specific primers, but rather encompass many billions upon billions primers of different nucleotide sequences.

At page 3 of the response it is asserted that a skilled artisan would not have arrived at the claimed invention as the artisan would have to ultimately select the appropriate primer sequence and that could be achieved through nothing less than luck. This argument has been fully considered and not been found persuasive towards the withdrawal of the rejection as the skilled artisan, or one of ordinary skill in the art at the time the invention was made would have to select upon the aforementioned nearly unlimited number of primers so to identify just which primers are in fact useful. Interestingly enough, applicant asserts that the determination of just which primers are useful is beyond the skill and capability of the ordinary artisan when the prior art teaches explicitly to select primers from highly conserved regions of HIV-1 LTR, yet when it comes to their own invention, the ordinary artisan is now somehow able to screen through the wasteland of billions of possible primers and select those that are now useful. With the skill being no different, and the results also being no different, one of ordinary skill in the art at the time the invention was made would be just as likely to arrive at useful primers that allow for the

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amplification of highly conserved regions in HIV-1 LTR as they would be to accurately screen through the myriad of applicant claimed primers and arrive at those that are useful.

For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephanie Zitomer can be reached on (703) 308-3985. The fax phone numbers for

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the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson
Bradley L. Sisson
Primary Examiner
Art Unit 1655

bls
July 28, 2001